

**REMARKS AND RESPONSE TO RESTRICTION**

Claims 1-61 were pending in the application. Claims 1-42, 49, 51-57, and 61 have been canceled without prejudice herein. Claims 43, 45-48, and 58-60 have been amended. New claims 62-78 have been added. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Support for the claim amendments and new claims can be found in the original claims and specification as filed. No new matter has been added by way of these amendments.

**RESTRICTION**

The Examiner has required restriction between the following inventions in the above-identified application:

Group I: Claims 1-41 and 58-60, drawn to an antibody that specifically binds to an epitope in the ligand/receptor binding domain of Cripto, classified in class 530, subclass 387.1.

Group II: Claim 42 and 49, drawn to a method of modulating growth of tumor cells in vitro in a sample, classified in class 435, subclass 7.1.

Group III: Claims 43, 44, 50 and 51, drawn to a method of modulating growth of tumor cells in vivo in a subject, classified in class 514, subclass 2, for example.

Group IV: Claims 45-48 and 52-55, drawn to a method of treating a subject having a tumor that over-expresses Cripto, classified in class 514, subclass 2, for example.

Group V: Claim 56, drawn to a method of determining whether a tissue expresses Cripto, comprising the step of analyzing tissue from the subject in an immunoassay using an antibody, classified in class 435, subclass 7.1 for example.

Group VI: Claim 57, drawn to a method of determining whether a cell line overexpresses Cripto, comprising the step of analyzing the cell line in an immunoassay using an antibody, classified in class 435, subclass 7.1 for example.

Group VII: Claim 61, drawn to a method of treating a subject for a condition associated with undesired cell proliferation, classified in class 424, subclass 9.1 for example.

If Applicants elect any one of Groups I-VII, the Examiner further requires a species election for the CRIPTO polypeptide sequence among the species of:

Species:       A)     SEQ ID NO: 1; or  
                  B)     SEQ ID NO:2.

The Examiner further requires selection of a single antibody from the list of claimed antibodies which is specific for the elected polypeptide sequence.

Further, if Applicants elect any one of Groups II-IV, the Examiner requires a species election for the tumor cell among the species of:

Species:       A)     breast;  
                  B)     testicular;  
                  C)     colon;  
                  D)     lung;  
                  E)     ovary;  
                  F)     bladder;  
                  G)     uterine;  
                  H)     cervical;  
                  I)     pancreatic; or  
                  J)     stomach.

Applicants hereby elect the Group III invention (Claims 43, 44, 50 and 51, drawn to a method of modulating growth of tumor cells in vivo in a subject) under 35 U.S.C. § 121 for prosecution on the merits, *with traverse*.

Further, Applicants elect the species of "SEQ ID NO: 1" and the single antibody produced by the hybridoma "B3F6.17" for search purposes only. Currently, claims 43-46, 48, 50, 58-60, and 62-73, and 76-77 are readable on these species. Applicants further elect the species of breast tumor cells for search purposes only. Currently, claims 43-48, 50, 58-60, and

62-78 are readable on this species. It is Applicants understanding that the search will be extended to the remaining species upon a finding of allowability.

Applicants traverse the restriction requirement to the extent that Groups III and IV should be reformed as a single group. Applicants' grounds for traversal are set forth below.

It is Applicants' position that claim 43 is generic to the claims of Groups III and IV. Claim 43 is directed to a method for modulating growth of tumor cells *in vivo* in a subject comprising the step of administering to the subject an effective amount of an antibody that binds Cripto. Claim 45 is directed to a method of treating a subject having a tumor, comprising administering an antibody that binds Cripto and includes the further limitation that the tumor over-expresses Cripto. Claim 43 is generic to Groups III and IV in that it embraces tumor cells generically, including cells that over-express Cripto.

Applicants' further argue that the inventions of Groups III and IV belong to the same search class (514) and the same subclass (2), and thus a literature search encompassing said groups would be nearly, if not completely, coextensive. In particular, Applicants submit that a search with respect to methods of modulating growth of tumor cells *in vivo* in a subject, comprising the step of administering an effective amount of an antibody that binds Cripto, would identify art relevant to the claims of Groups III and IV. In view of the relatedness of the claimed subject matter, it is Applicants' position that search and examination of Groups III and IV would not constitute an undue burden to the Examiner. In light of these arguments, Applicants propose that Groups III and IV be reformed into a single group, newly formed Group III, comprising claims 43-48, 50, 58-60, and 62-78, drawn to methods of modulating growth of tumor cells *in vivo* in a subject comprising the step of administering an antibody that binds Cripto.


Applicants reserve the right to traverse the restriction between the non-elected groups in this or a separate application.

**CONCLUSION**

If a telephone conversation with the Applicant's Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at 617-227-7400.

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Respectfully submitted,

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